Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 37 and 41 under 35 U.S.C. § 112, first paragraph, as lacking written descriptive support is respectfully traversed in view of the above amendments and the following remarks.

The U.S. Patent and Trademark Office ("PTO") has taken the position that claims 37 and 41 are not adequately described in the specification because they are not drawn to any specific polymorphisms of the Hox A1 and Hox B1 polypeptides. For the reasons noted below, applicants respectfully submit that amended claims 37 and 41 are adequately described in the specification.

Claim 37 as amended recites an isolated polypeptide that includes "the amino acid sequence of SEQ ID NO: 2" and has "a single amino acid substitution of the histidine at position 73." Thus, the polymorphism recited in claim 37 is drawn to a single amino acid at position 73 of the Hox A1 polypeptide. The representative species is a His→Arg substitution at position 73, which is shown to be a genetic marker for autism (page 25, lines 24-31). Since there are only 20 amino acids, the genus consists of 19 amino acid substitution species. It is well known in the art of molecular biology that a single mutation in a polypeptide chain can alter protein folding, and thereby alter protein functionality. This is particularly true when the amino acid being substituted varies with respect to charge and polarity. Surprisingly, the His→Arg genetic marker for autism is a substitution of one positively charged polar amino acid for a second positively charged polar amino acid. Thus, a skilled practitioner in the art would recognize that the substitution of other amino acids at position 73 would likely alter Hox A1 function, and thereby constitute a genetic marker for autism, particularly when the amino acids being substituted vary with respect to polarity and/or charge (e.g., His→Ala). Therefore, the His→Arg substitution adequately represents the claimed genus of Hox A1 polymorphisms.

Claim 41 as amended recites an isolated polypeptide that includes "the amino acid sequence of SEQ ID NO: 6" and has "a three amino acid insertion between the amino acids at positions 27 and 28." Thus, the polymorphism recited in claim 41, is drawn to a three-amino acid insertion at a single site (between amino acids 27-28) in the Hox B1 polypeptide. The representative species is a His-Ser-Ala insertion between positions 27 and

28, which is shown to be a genetic marker for autism (page 13, line 48 to page 14, lines 1-3). Although the genus consists of many three-amino acid combination species, it is commonly known in the art of molecular biology that missense mutations (mutations causing an alteration in the amino acid sequence) generally alter protein function, regardless of the specific amino acid alterations, particularly when the missense mutation is an insertion that alters the total number of amino acids in the polypeptide chain. Thus, a skilled practitioner in the art would recognize that the insertion of other three-amino acid combinations between positions 27 and 28 would also alter Hox B1 function, and thereby constitute a genetic marker for autism. Therefore, the His-Ser-Ala insertion adequately represents the claimed genus of Hox B1 polymorphisms.

The PTO has also taken the position that claims 37 and 41 are not adequately described in the specification because they are not limited to polypeptide fragments encoded by any particular part of *Hox A1* or *Hox B1*. This rejection is rendered moot with respect to claims 37 and 41 in light of the above amendments. New claims 45 and 47 have been added, and support for these claims is found in the present application at page 22, lines 26-32. Because a person with skill in the art is capable of envisioning the full length Hox A1 and Hox B1 polypeptides and their respective polymorphisms, a person with skill in the art is also capable of envisioning the polypeptide fragments of new claims 45 and 47.

For all the reasons above, applicants respectfully submit that the present application provides adequate written descriptive support for the presently claimed subject matter. Therefore, the rejection of claims 37 and 41 for lack of written descriptive support should be withdrawn.

The rejection of claims 37 and 41 under 35 U.S.C. § 102(b), as being anticipated by GenBank Accession No. A30242 ("A30242") is overcome by the amendments to claims 37 and 41. In particular, the protein identified in A30242 fails to satisfy all limitations recited in claims 37 and 41. Therefore, this rejection should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: December 3, 2003

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450, on the date below.

Date 12/3/03 Wendy L. Barry